

**Remarks**

Claims 1-31, 37 and 38 have been amended and claim 39 has been cancelled without prejudice or disclaimer of the encompassed subject matter. The amendment to claim 1 addresses the substituents available for recited variables  $R^1$ ,  $R^{1a}$ ,  $R^2$ ,  $R^{2a}$ ,  $R^3$  and  $R^4$ . The amendment to claim 38 identifies the tumor to be treated as a breast tumor. Applicants submit that these amendments are fully supported by the specification as originally filed. All additional amendments to the claims are formalistic in nature and are intended to add further clarity to the recited subject matter. Accordingly, Applicants submit that no prohibited new matter has been added by any of the amendments.

**1. Technically Related Applications**

Applicants would like to bring to the Examiner's attention the following applications with the same assignee that may be considered to be technically related.

<b>Inventor</b>	<b>U.S. Application No. Filing Date</b>	<b>Examination Status</b>
Hennequin <i>et al.</i>	10/494,137 October 6, 2004	abandoned
Hennequin <i>et al.</i>	10/494,388 October 1, 2004	abandoned
Bradbury <i>et al.</i>	10/571,851 March 15, 2006	response filed
Bradbury <i>et al.</i>	10/572,262 March 16, 2006	response filed
Hennequin <i>et al.</i>	10/578,663 January 17, 2007	office action mailed
Hennequin <i>et al.</i>	11/283,415 November 21, 2005	response filed
Hennequin <i>et al.</i>	11/443,208 May 31, 2006	unexamined
Hennequin <i>et al.</i>	11/443,395 May 31, 2006	unexamined
Bradbury <i>et al.</i>	11/628,011 November 30, 2006	unexamined
Barlaam <i>et al.</i>	11/792,921 June 13, 2007	unexamined

Inventor	U.S. Application No. Filing Date	Examination Status
Bradbury	11/817,391 August 29, 2007	unexamined
Bradbury	11/817,393 August 29, 2007	unexamined
Bradbury	11/912,792 October 26, 2007	unexamined
Bradbury	11/912,794 October 26, 2007	unexamined
Bradbury	12/067,415 March 19, 2008	unexamined
Bradbury <i>et al.</i>	12/067,416 March 19, 2008	unexamined
Barlaam <i>et al.</i>	12/095,665 May 30, 2008	unexamined
Barlaam <i>et al.</i>	12/095,659 May 30, 2008	unexamined

## 2. Information Disclosure Statement

The Examiner indicates that Applicants' earlier submitted Information Disclosure Statements of June 8, 2007; January 28, 2008; February 27, 2007; and October 24, 2005 require inventor names to be entered for all of the listed foreign documents.

Applicants respectfully disagree that entry of the inventor names is required for foreign documents listed on a PTO-1449 form and point to 37 C.F.R. 1.98(b)(4), which states that

Each foreign patent or published foreign patent application listed in an information disclosure statement must be identified by the country or patent office which issued the patent or published the application, an appropriate document number, and the publication date indicated on the patent or published application.

No mention is made in the above passage of any requirement of listing each inventor name. In contrast, 37 C.F.R. 1.98(b)(1), which addresses U.S. patents, states that

Each U.S. patent listed in an information disclosure statement must be identified by inventor, patent number, and issue date.

In view of the above, Applicants respectfully request that this objection be withdrawn.

**3. Rejection under 35 U.S.C. 112, second paragraph**

Claims 1-9, 16-30, 32 and 37-39 are rejected as allegedly indefinite for the following reasons asserted by the Examiner:

- A. “wherein any CH,...optionally bears...one or more...”

The Examiner indicates that the above-identified phrase is unclear “if it means for the first carbon to be  $>C=O$  because CH bearing alkanoyl would still have incomplete valence.”

While Applicants respectfully disagree with the Examiner regarding the clarity of the above-recited phrase, Applicants submit that in view of the amendments to claim 1 that remove alkanoyl as a possible substituent for CH, this rejection has been effectively mooted.

- B. “converting a quinazoline derivative of the formula I into another quinazoline derivative of the formula I”

The Examiner indicates that the above-identified phrase as recited in claim 37 is unclear as to “derivative is converted into which.”

Applicants submit that a person of ordinary skill in the art would understand the meaning of the contested phrase and would have sufficient knowledge to chemically convert a compound encompassed by generic formula I into a different compound that is still encompassed by generic formula I. For example, a person of ordinary skill in the art would know how to protect a hydroxy or amino group present in a compound of formula I to generate the corresponding protected alcohol or amine that is still encompassed by formula I. Accordingly, Applicants respectfully request that this rejection be withdrawn.

- C. “...treating a tumour sensitive to inhibition of the erbB2...”

Claim 38 is rejected as indefinite due to the above recitation.

While Applicants do not acquiesce to the merits of this rejection, Applicants have eliminated this phrase in claim 38 via amendment. Accordingly, Applicants respectfully request that this rejection be withdrawn.

D. "...method for selectively inhibiting erbB2 receptor tyrosine kinase..."

Claim 39 is rejected as indefinite due to the above recitation.

While Applicants do not acquiesce to the merits of this rejection, Applicants have cancelled claim 39 without prejudice or disclaimer of the encompassed subject matter. Accordingly, Applicants submit that this rejection has been effectively mooted.

**4. Rejection under 35 U.S.C. 112, first paragraph**

A.  $-NR^3R^4$

Claims 1-9, 16-30, 32 and 37-39 are rejected as lacking enablement due to the recited scope of  $-NR^3R^4$ . The Examiner indicates that while the specification is enabling for compounds of formula I wherein  $-NR^3R^4$  is a dialkylamino, it "does not reasonably provide enablement for making and using the remaining compounds of formula I." An analysis of each of the *In re Wands* factors is provided by the Examiner in support of this assertion.

While Applicants do not acquiesce to the merits of this rejection, Applicants have amended claim 1 to reduce the scope of the contested  $-NR^3R^4$  group such that each of  $R^3$  and  $R^4$ , which may be the same or different, is selected from (1-3C)alkyl and (2-4C) alkenyl, wherein any CH or CH<sub>2</sub> or CH<sub>3</sub> within any of  $R^1$ ,  $R^{1a}$ ,  $R^2$ ,  $R^{2a}$ ,  $R^3$  and  $R^4$  optionally bears on each said CH or CH<sub>2</sub> or CH<sub>3</sub> a substituent selected from hydroxy and (1-3C)alkoxy. As representative support for  $R^3$  or  $R^4$  being alkenyl, Applicants point to page 9 of the corresponding PCT application wherein exemplary alkenyl groups are listed at line 5 (e.g., vinyl, isopropenyl, allyl and but-2-enyl) and to the compounds of original claim 31 listed at page 126, lines 15-16 and 25-26. As representative support for the optional substituents of hydroxy and alkoxy, Applicants point to the compounds of original claim 31 as recited in the corresponding PCT application listed at page 124, lines 23-24 and 27-28 and at page 126, lines 19-20.

The Examiner indicates on page 5 of the current Office Action that "...a skilled chemist would not be able to extrapolate from the synthetic procedures of the disclosure to make compounds of formula I with many of the moieties instantly claimed for  $R^3$  and  $R^4$ ." Applicants respectfully disagree with this assertion and point to page 127 of the corresponding PCT application, where scheme (c) of process claim 37 shows that a simple generic amine depicted as

formula VII reacts with a quinazoline of formula VI to provide a compound of formula I. As the Examiner can appreciate, there are hundreds of amine compounds of the formula VII (*i.e.*, with widely varying  $R^3$  and  $R^4$  groups) that are readily available either commercially or from prior art preparations. Scheme (d) of process claim 37 shows that the amine of formula VII can also react with a quinazoline of formula VIII to provide a compound of formula I. Accordingly, Applicants submit that the specification adequately provides at least two methodologies of preparing compounds of formula I from readily available amines (of structure VII) capable of containing diverse  $R^3$  and  $R^4$  groups. For at least the above-discussed reasons, Applicants submit that claim I as amended relative to  $-NR^3R^4$  is enabled by the specification and therefore respectfully request that this rejection be withdrawn.

**B. Claims 38 and 39**

Claims 38 and 39 are rejected as lacking enablement for the reasons given at pages 6-10 of the current Office Action. The Examiner does indicate that the specification is enabling for a method of treating a breast tumor.

While Applicants do not acquiesce to the merits of this rejection, Applicants have, in order to expedite allowance of the subject application, amended claim 38 to recite the treatment of a breast tumor and cancelled claim 39 without prejudice or disclaimer of the encompassed subject matter. Accordingly, Applicants respectfully request that this rejection be withdrawn.

**5. Allowable Claims**

Claims 10-15 and 31 are objected to as being dependent upon a rejected base claim, but is indicated as being allowable if rewritten in independent form, including all of the limitations of the base claim and any intervening claims.

In view of the amendments and remarks presented in this response, Applicants submit that all of the pending claims should now be in a condition for allowance.

**6. Conclusion**

The foregoing amendments and remarks are being made to place the application in a condition for allowance. Applicants respectfully request reconsideration and the timely


allowance of the pending claims. Should the Examiner find that an interview would be helpful to further prosecution of this application, she is invited to telephone the undersigned at her convenience.

**Except** for issue fees payable under 37 C.F.R. 1.18, the Commissioner is hereby authorized by this paper to charge any additional fees during the entire pendency of this application including fees due under 37 C.F.R. §§ 1.16 and 1.17 which may be required, including any required extension of time fees, or to credit any overpayment to Deposit Account 50-0310. This paragraph is intended to be a **Constructive Petition for Extension of Time** in accordance with 37 C.F.R. 1.136(a)(3).

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Respectfully submitted  
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